CHAPTER 24

Craniofacial Fibrous Dysplasia

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DEFINITION AND CLASSIFICATION

Fibrous dysplasia of bone (FD) is an uncommon condition in which normal bone and bone marrow are replaced by a distinct benign fibro-osseous tissue.[1, 2] It may occur anywhere in the craniofacial, axial, or appendicular skeleton; however, the sites most commonly involved are the skull base and proximal femur. When a single skeletal site is involved the term *monostotic fibrous dysplasia* (MFD) is applied, and when multiple skeletal sites are involved the term *polyostotic fibrous dysplasia* (PFD) is used. In MFD, the craniofacial region is the site most commonly involved.[3] The McCune-Albright syndrome consists of the triad of PFD, café-au-lait skin pigmentation, and precocious puberty (or other hyperfunctioning endocrine states such as hyperthyroidism, growth hormone excess, and so on).[4, 5] These classifications are somewhat arbitrary, in that most would consider FD isolated to the craniofacial region and involving more than one adjacent bone to be MFD. Likewise, FD (MFD or PFD) may be associated with café-au-lait skin pigmentation without precocious puberty, bone disease may occur without skin findings but with hyperfunctioning endocrinopathies, and skin and endocrine findings may exist in the absence of bone disease.[6] Combinations of skin, bone, and endocrinopathies other than the classic triad of café-au-lait, PFD, and precocious puberty may be considered variants of McCune-Albright syndrome.

NATURAL HISTORY

When manifested early in life, craniofacial FD is often associated with McCune-Albright syndrome or a variant of this syndrome.[7, 8] These cases usually take a more aggressive course, and significant morbidity may develop, including blindness or other ocular problems, deafness, dental or swallowing difficulties, or deformity. However, in most cases, the progression is slow and vital structures are often spared in spite of extensive FD (Fig. 24–1). Through regular screening examinations, problems can be detected in a sub- or early clinical state. The regular examination should include a nonenhanced computed tomographic (CT) scan of the head, neuro-ophthalmologic examination, and hearing testing,[9] and it should be performed annually, but more

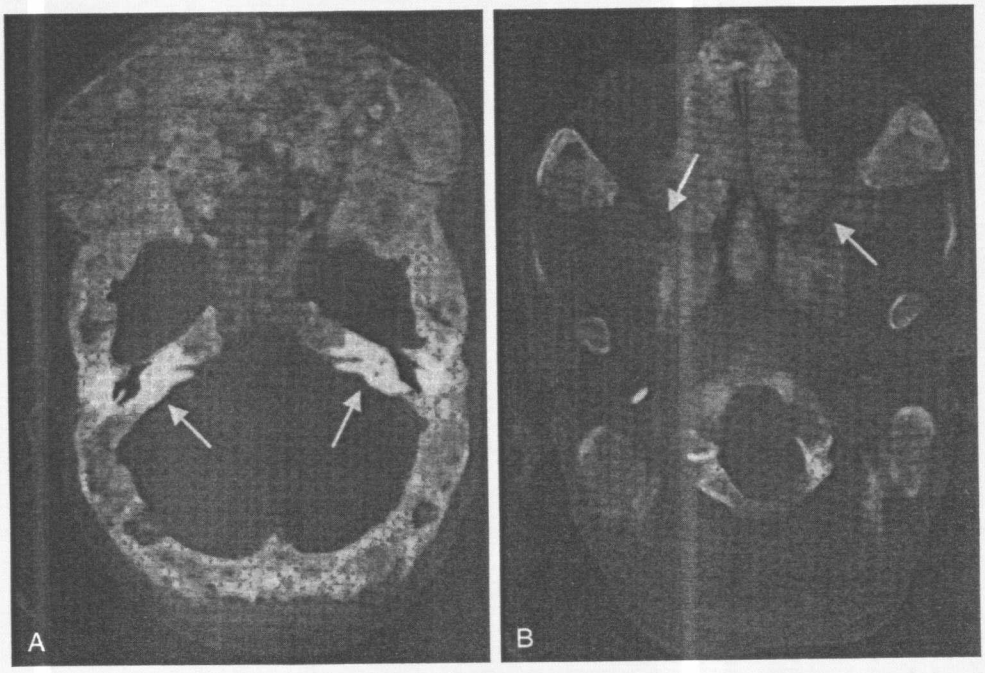

Figure 24–1. Vital structure sparing in massive craniofacial FD. Selected images of a computed tomographic scan of the skull of a patient with massive craniofacial FD are shown. Virtually every craniofacial bone but the petrous bone is involved. In spite of this degree of involvement, key vital structures are spared. *A*, Petrous ridge and auditory canal sparing *(arrows)*. *B*, Optic nerve sparing *(arrows)*.

frequently if problems have been detected. The most common problems necessitating craniofacial surgery are visual disturbances, hearing loss, deformity, or intractable pain.

On occasion, a significant change can occur suddenly and progress rapidly. This is frequently associated with the development of a cystic lesion (aneurysmal bone cyst, or a variation thereof) within a preexisting FD lesion.[10] When symptoms appear suddenly, a CT scan of the skull should be performed. The detection of a symptomatic, new cystic lesion within preexisting FD, or other new findings, should be addressed immediately.

Isolated craniofacial FD may present later in life as an incidental finding detected on an imaging study performed for other reasons.[9] In these cases, the FD is usually of little or no clinical significance. At most, these patients present with a history of headaches or sinus infections. If the lesions are in a typical location and have a typical radiographic appearance,[3, 11, 12] they may be followed on an annual basis initially, and less frequently with time.[9] Concern over the certainty of diagnosis may be allayed by demonstration of features of FD in a biopsy specimen.

Rarely, FD may undergo degeneration to a sarcoma.[13] In the past, when attempts were made to treat FD with external-beam radiation, sarcomatous degeneration was not uncommon. In the modern era, with external-beam radiation having been abandoned as ineffective and dangerous, the frequency of sarcomatous degeneration has dropped to less than 1%.[13] However, when sarcomatous degeneration does occur, the craniofacial region is a common site. The signs and symptoms of the development of a sarcoma are a rapidly expanding mass in an area of preexisting FD. On CT, this appears as a soft tissue mass within an area of preexisting FD that lacks the typical imaging features of FD and that has eroded and replaced the normal bony cortex[14] (Fig. 24–2).

Questions remain over what initiates and/or promotes the progression of craniofacial FD. Some clinicians have suggested hormonal changes of adolescence[15] or pregnancy[16] are contributory. The accuracy of this observation is unclear, given that in many of these patients, owing to the precocious puberty of McCune-Albright syndrome, sometimes manifested within the first year of life, the normal chronologic age of "puberty" is not applicable. Whether pregnancy actually promotes progression is also not clear. It is possible that FD lesions may grow during pregnancy given the fact that FD lesions are highly vascular[17] and that there are elevated levels of angiogenic factors in the maternal circulation during pregnancy.[18] Although there are isolated case reports in the literature of progression in FD in pregnancy,[19] in our series of patients we have had as many cases remain quiescent or improve during pregnancy as those that progress (unpublished observations).

Fibrous dysplastic lesions may retain hormonal responsiveness inherent in normal bone, and it is therefore possible that certain hormonal states may exacerbate FD. Growth hormone excess can fuel the growth of FD, especially in the craniofacial bones.[20] Although it has not been extensively investigated, it is likely that FD lesions are also worsened by thyrotoxicosis, hyperparathyroidism, glucocorticoid excess, and abnormalities of phosphate metabolism. Therefore, it is essential that all patients with FD be evaluated to rule out coexisting endocrinopathies. Whereas FD lesions in the axial and appendicular skeleton, particu-

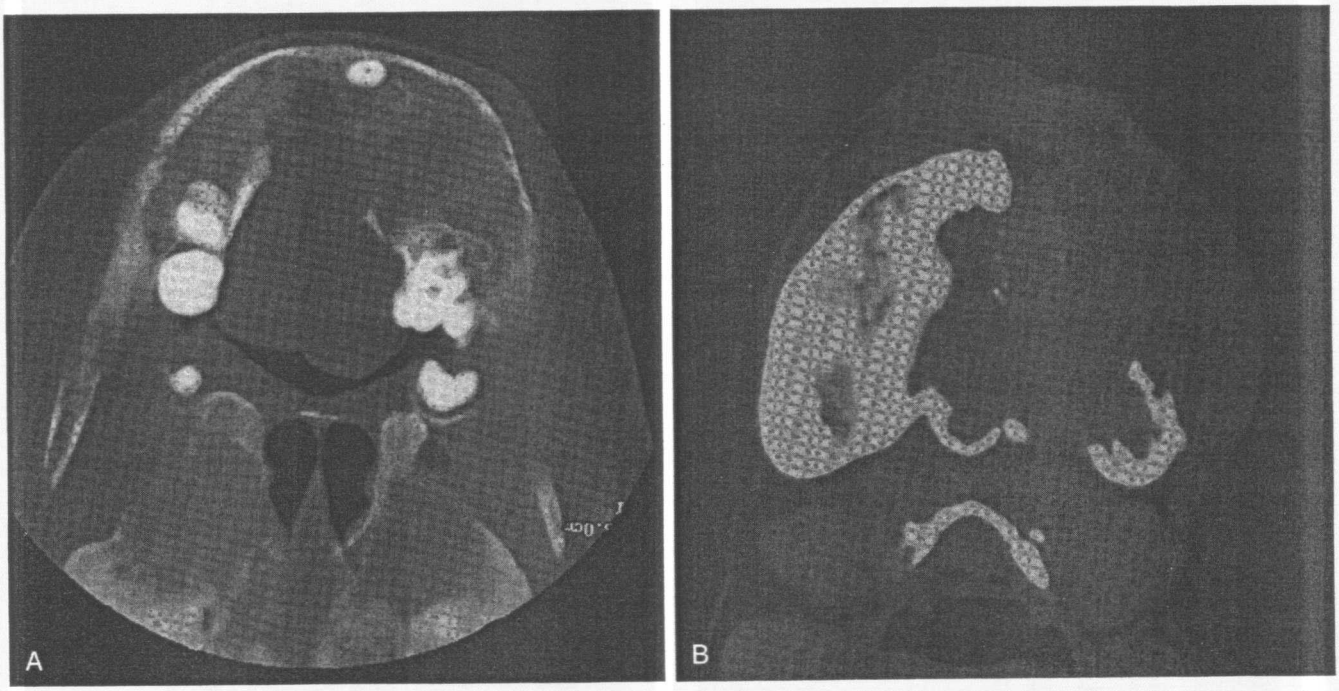

Figure 24–2. Computed tomographic scans of the mandible of an 11-year-old girl with McCune-Albright syndrome who developed a sarcoma in a preexisting FD lesion. *A*, Scan (bone window) of the mandible performed in 1998 demonstrating typical ground-glass appearance of FD. *B*, The same area 1 year later (soft tissue window) demonstrating loss of the bone cortex and an expansile soft tissue mass.

larly of the lower extremities, tend to become less active with age, this is not the case with craniofacial FD. These lesions tend to remain active, and morbidity continues through adulthood.[21]

GENETICS

The McCune-Albright syndrome is a noninherited genetic disease caused by point mutations of the alpha subunit of the Gs (stimulatory) protein.[22, 23] These mutations consistently affect a single codon in exon 8, replacing the Arg201 in the Gs protein with a cysteine or a histidine, resulting in a "gain-of-function," dominant negative, molecular defect. Less frequently, other amino acids, such as glycine[24] or serine[25] are substituted for the Arg201. Interestingly, the phenotypic effects of activating GNAS1 mutations seem to be the same, regardless of the type of amino acid substituting for Arg201. Because the activating GNAS1 mutations were originally identified in endocrine tumors (in which alternative activating mutations have also been demonstrated in the codon for Gln227 as well as Arg201), the mutated Gs alpha allele was initially regarded as the product of an oncogene (*Gsp*).[26] More recently, it has become clear that the polyostotic and monostotic forms of FD occurring as isolated skeletal disorders are consistently, if not always, associated with this same genetic abnormality.[27–30] A whole spectrum of clinical conditions, ranging from isolated endocrine tumors to isolated skeletal lesions to variable combinations thereof, are thus thought to be the result of a common genetic abnormality.

Based on the lack of any evidence of germline transmission of the GNAS1-activating mutations, it was postulated that postzygotic mutational events would allow for the survival of an otherwise lethal gene.[31] Somatic mosaicism was later demonstrated as the genetic basis for McCune-Albright syndrome and its associated disorders. The postzygotic occurrence of GNAS1 mutation fully explains the distribution of mutated cells through all three germ layers leading to skin hyperpigmentation and craniofacial FD (ectoderm and neuroectoderm), axial and appendicular fibrous dysplasia (mesoderm), and various endocrinopathies (endoderm) (Fig. 24–3). It is of interest to note that craniofacial bones are derived from a different embryonic layer (neuroectoderm) from axial and appendicular bones (mesoderm).

The observation that affected tissues arise from all three embryonic germ layers has been invoked to explain the diverse phenotypic (clinical) expression of the genetic abnormality.[32, 33] According to this hypothesis, McCune-Albright syndrome and PFD would represent the widespread distribution of the mutated allele resulting from a mutational event that occurred very early in development. In contrast, MFD, as well as isolated endocrine misfunction or tumors, would represent a somatic mutation that occurred later in development, perhaps even postnatally, within a localized population of diversified cell types. An alternative hypothesis would be that mutated cells experience different rates of cell death during embryonic and postnatal development, resulting in variable loads of mutated cells in various tissues of an affected individual.

The stimulatory G protein, Gs, is a key regulatory element of the cyclic adenosine monophosphate (AMP) dependent signaling pathway. After binding of ligand to the Gs alpha–coupled receptor, the Gs alpha–mediated step of signal transduction begins with the displacement of protein bound guanosine diphosphate by guanosine triphosphate (GTP), which allows for association with adenylyl cyclase, thereby stimulating cyclic AMP production. Subsequently, the inherent GTPase activity of Gs alpha hydrolyzes the GTP, causing dissociation from adenylyl cyclase and cessation of cyclic AMP production.[34] In the mutated Gs alpha subunit, the GTPase activity is reduced by 30-fold to 100-fold and the cyclic AMP pathway remains activated.

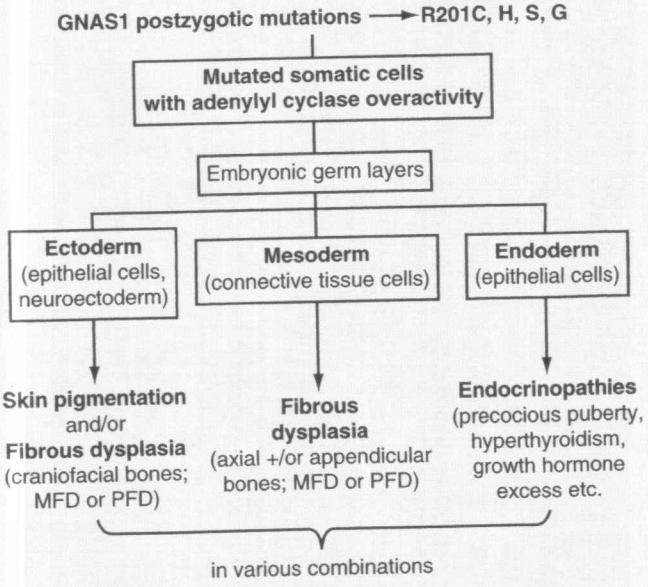

Figure 24–3. Relationship between GNAS1 mutations and phenotype. The phenotype of the affected patient is determined by and when and in which germ layer in development the activating mutation occurs. Almost any combination can be observed.

CELL BIOLOGY AND MOLECULAR PATHOPHYSIOLOGY

As in endocrine tissues, the phenotypic expression of GNAS1-activating mutations in the skeleton is believed to be the result of inappropriate cyclic AMP stimulation of bone cells. Activating GNAS1 mutations have been identified in FD tissue,[27, 35–37] and excess production of intracellular cyclic AMP has been demonstrated in FD cells in vitro.[38]

Critical to understanding the nature of FD is the recognition of the osteogenic phenotype and nature of the so-called fibrous tissue that characterizes the lesion.[2] This allows for a more precise classification of FD as an osteogenic cell disease rather than a fibrous disorder of bone.[39] "Fibroblastic" cells found in FD indeed exhibit a number of properties of osteogenic progenitors, both in vivo and in vitro. Normally, osteogenic progenitors can be isolated from the bone marrow as adherent, clonogenic, and fibroblast-like cells (i.e., colony forming unit-fibroblasts [CFU–F]).[40–42] After their isolation and expansion ex vivo, the progeny of CFU–F (bone marrow stromal cells) are

able to differentiate into different cell types, including osteoblasts, chondrocytes, myelosupportive stromal cells, and adipocytes.[43–45] High numbers of such cells are isolated from the abnormal, fibrotic marrow of FD lesions.[46] Thus, the characteristic fibrous tissue of FD can be viewed as the abnormal accumulation of osteogenic progenitors.

The significance of mutated osteoprogenitor cells in the development of an FD lesion is illustrated by the ability of ex vivo expanded bone marrow stromal cells isolated from FD to recapitulate the lesion on transplantation into immunocompromised mice.[46] Under the same experimental circumstances, normal bone marrow stromal cells generate a miniature replica of the bone/bone marrow organ, whereas cells from FD generate a miniature replica of FD. Interestingly, these studies have emphasized that the population of osteoprogenitor cells that are isolated from an individual FD lesion are a mixture (a mosaic) of normal and mutated cells, rather than a clonal population with the abnormal genotype. In the in vivo transplantation assay, a mosaic strain of normal and mutated osteoprogenitor cells generates an FD-like structure, whereas pure populations of mutated cells are lost from the graft. This suggested that even in the generation of an individual FD lesion, the abnormal genotype is indeed lethal and may only remain viable and pathogenically effective due to a "nursing" effect of coexistent normal cells.

In the native FD lesion, as well as in its experimental in vivo model, the abnormal osteogenic cells give rise to an abnormal pattern of bone formation. Bone formed within FD is abnormal both in structure and chemical composition of its organic matrix and represents the output of abnormal, mature osteoblasts that differentiated from abnormal osteoprogenitor cells. The entire osteogenic lineage, from progenitor cells to the mature osteoblasts, is thus affected by the consequences of GNAS1 mutations and excess cyclic AMP. Furthermore, these misfunctioning osteoblasts are unable to further develop into the stroma that is required to support hematopoiesis and subsequent adipogenesis. Consequently, normal marrow is replaced by accumulated osteoprogenitors and abnormal bone.

The immediate downstream consequences of excess cyclic AMP in osteogenic cells are incompletely understood. Some changes observed in vivo can be directly mimicked by in vitro models as direct effects of excess cyclic AMP. For example, the cytoskeletal derangement expressed in vivo by the typical retracted morphology observed in osteoblasts in FD can be reproduced in normal osteogenic cells in vitro by the exogenous addition of cell-permeant analogues of cyclic AMP[2] (Fig. 24–4*B*). More subtle events that are directly associated with the cyclic AMP–mediated disruption of the cytoskeleton in osteogenic cells remain to be dissected. In general terms, they are known to include the dysregulation of cellular pathways that are critical for cell survival and for its proper interaction with the extracellular environment.

Overexpression of c-*fos* in FD cells in vivo has been reported,[37] and it could be seen as a possible mediator of excess cell proliferation in osteogenic cells ultimately leading to accumulation of "fibrous" cells.[29] However, the actual rates of cell growth in FD have remained controversial and have never been assessed directly in situ.

Other studies have implicated excess production of interleukin-6 as a critical downstream effect of GNAS1 mutations.[38] Again, although excess interleukin-6 production would fit the profile of a mediator of some aspects of FD pathology (e.g., increased bone resorption), more evidence is required before this effect can be conclusively recognized as an inherent consequence of the abnormal genotype.

HISTOPATHOLOGY

In general terms, all FD lesions consist of the replacement of normal bone and marrow with abnormal bone and fibrous tissue. As mentioned earlier, bone in an individual FD lesion is abnormal in structure and composition.[2] When illuminated by polarized light, FD bone is woven in texture. Peculiar systems of collagen bundles running perpendicular to the surface of bone trabeculae and resembling Sharpey

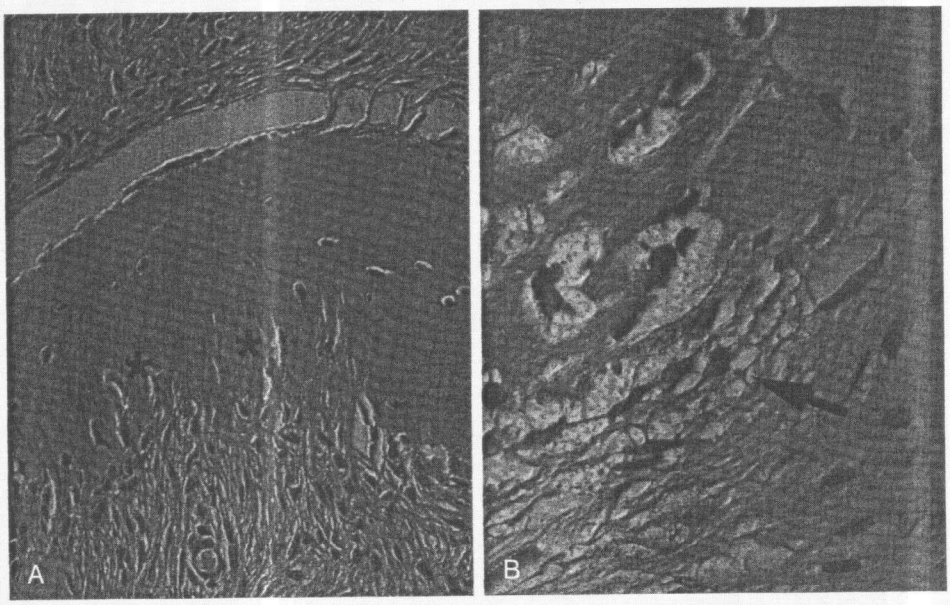

Figure 24–4. Typical histologic features of FD. *A*, Systems of collagen fibers perpendicular to bone surfaces (Sharpey fibers, *asterisks*) represent a recurrent finding in FD lesions. *B*, Retracted morphology of osteoblastic cells at forming bone surfaces (*arrow*). This characteristic histologic change represents an immediate effect of excess cyclic adenosine monophosphate in osteogenic cells and can be reproduced in normal osteogenic cells in vitro by the addition of cell-permeant cyclic adenosine monophosphate analogues.

fibers are a characteristic feature of FD bone (see Fig. 24–4*A*). The abnormal bone is enriched in osteonectin but deficient in other matrix proteins found in normal newly formed bone, such as bone sialoprotein. The fibrous tissue filling the space between abnormal bone trabeculae consists of "fibroblastic" cells that resemble normal preosteoblasts by virtue of their expression of alkaline phosphatase and a host of characteristic matrix proteins. Yet unlike their counterparts in normal marrow (Westen-Bainton cells, reticular cells),[46a] they fail to support the homing, growth, and maturation of hematopoiesis.

This basic histologic theme—abnormal bone and replacement of hematopoietic marrow with a nonhematopoietic fibrous tissue—is highly variable in individual FD lesions. Appreciation of the variability of the histology of individual FD lesions has important implications not only for the diagnosis of the disease but also for the progression of the disease. Determinants of these histologic variations on the theme include secondary events (e.g., intralesional hemorrhage leading to aneurysmal bone cysts); site-specific features between craniofacial, axial, and appendicular bone; biologic age of the individual lesion; age of the patient; and possibly superimposed hormonal influences. It is equally important to appreciate that some of the statements that are commonplace in textbooks of bone pathology may be inaccurate and misleading. For example, the abnormal bone formed in FD is not "metaplastic" but the direct output of true (although abnormal) bone-forming cells. "Osteoblastic rimming" of the abnormal bone trabeculae may be hard to detect as usually reported, because of the abnormal morphology of FD osteoblasts, whose retracted cell shape is notably different from the usual cuboidal osteoblast morphology.

Craniofacial lesions of FD are themselves notably distinct from FD lesions occurring at other skeletal sites (Fig. 24–5). As opposed to FD lesions in the appendicular skeleton, they tend to be sclerotic on radiographic examination,[47, 48] as reflected by a high bone to fibrous tissue ratio.[49] Lesions occurring in the gnathic bones exhibit a peculiar histologic pattern, in which bone trabeculae run parallel to one another, contain high numbers of abnormal osteocytes, and are lined by easily detectable rows of osteoblasts residing on the same side of each trabecula (see Fig. 24–5*B*). Difficult to recognize as a typical FD pattern at first glance, this histologic variant emphasizes how divergent craniofacial FD lesions can be from the typical "Chinese writing" appearance in the axial skeleton. Although lesions of the cranial base are also sclerotic, they tend to resemble pagetic bone, both histologically as well as radiographically. Hallmarks of this site-specific variant include complex systems of cement lines (resembling Schmorl's mosaic), a common feature in Paget's disease. It is currently not understood why craniofacial lesions are distinctly sclerotic as opposed to the lytic lesions seen in the appendicular skeleton, but this may be related to their different embryonic origin (neuroectodermal as opposed to mesodermal).

Histologic evidence of bone resorption (osteoclasts on bone surfaces) is also variable in FD and ranges from normal to extremely high. At times, lesions indistinguishable from brown tumors of hyperparathyroidism can be observed and may account for a predominantly lytic appearance of a lesion. The latter appearance may also reflect the occurrence of a cystic change after intralesional hemorrhage, which appears to be particularly common in craniofacial bones.[10, 50] In spite of the inherent benign nature of FD lesions, the development of cystic lesions with intralesional hemorrhage and rapid expansion may have disastrous consequences, such as compression of cranial nerves or other vital structures.

FUTURE DIRECTIONS

Clearly, there is a need for an increased understanding of the pathogenetic mechanisms of FD to develop better therapies. Comprehension of how constitutive cyclic AMP production affects the cellular and molecular mechanisms of osteogenic cell proliferation and differentiation is needed. Focus on the downstream effectors and regulators of cyclic AMP signaling, protein kinase A (PKA) and phosphodiesterase, may provide great insight, as well as point the way to more effective therapies. Likewise, increased knowledge of bone marrow stromal cell biology in general will undoubtedly impact not only on understanding the disease but also in treating it. The use of bone marrow stromal cells in tissue engineering is currently an active area of research and shows great promise. Extirpation of mutated cells from FD lesions, physically and/or medicinally, followed by repopulation with nonmutated cells, expanded and/or modified ex vivo, offers a potentially exciting treatment option in the not-too-distant future.

CLINICAL TREATMENT OPTIONS

Medical Management

The medical management of FD, particularly in the craniofacial region, appears to have little impact on the course of the disease. Early attempts at treatment, which included chemotherapy, glucocorticoids, calcitonin, and radiation, were unsuccessful.[51, 52] In fact, as stated earlier, irradiation clearly promotes sarcomatous degeneration of FD and should never be attempted. This must be kept in mind when giving consideration to the treatment of pituitary lesions (growth hormone–secreting adenomas). Because of the high level of bone resorption observed in some lesions, there have been a number of small uncontrolled trials using the bone resorption–inhibiting bisphosphonate pamidronate to treat mixed groups of patients (McCune-Albright syndrome, PFD, MFD).[53, 54] The most consistent results from these trials were a decrease in pain and in the biochemical markers of bone turnover. These data are difficult to interpret for several reasons: (1) the trials were uncontrolled, (2) pain associated with FD is known to wax and wane, and (3) bisphosphonate treatment of any individual (normal or with a disease) will decrease biochemical markers of bone turnover. Importantly, these studies do not comment on the effect of treatment on craniofacial FD. Our personal experience is that the beneficial effect of bisphosphonates on craniofacial FD is at best limited.

Pain control is often an issue in craniofacial FD. While

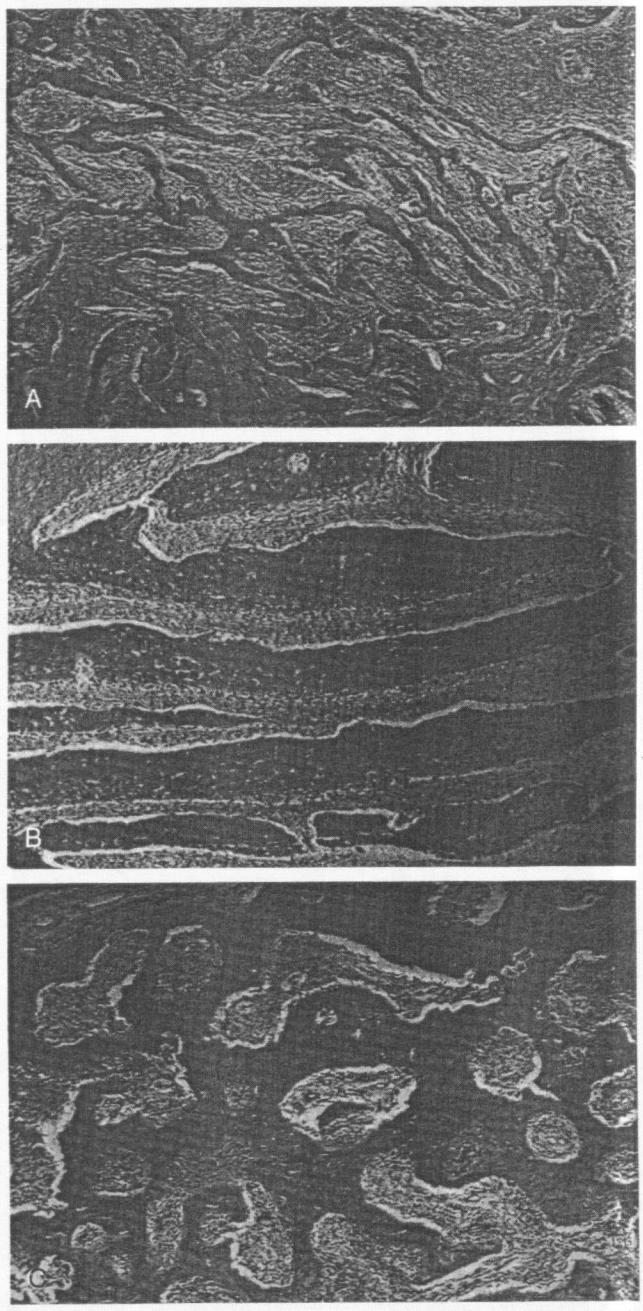

Figure 24–5. Microscopic appearance of FD from different skeletal sites. *A*, Classic "Chinese writing" FD typically observed in lesions from the axial and appendicular skeleton. The pathologic tissue is characterized by thin and disconnected bone trabeculae in an abundant fibrous background. *B* and *C*, FD of craniofacial bones. The more sclerotic appearance is due to the higher ratio of bone to fibrous tissue. The pathologic bone is deposited as disconnected and parallel trabeculae in FD affecting the gnathic bones *B*, whereas lesions of the cranial base are characterized by a continuous network of thick bone trabeculae (*C*).

nonsteroidal antiinflammatory drugs can often be effective, narcotic analgesics, sometimes on a regular basis and in relatively high doses, are sometimes required. Occasionally, anticonvulsants with analgesic properties are helpful either as single agents or in combination with other classes of analgesics. Referral to a pain specialist is frequently necessary.

Surgical Management

Nonoperative pharmacologic management of craniofacial FD is still experimental and limited, thus making surgery the best treatment option presently available; however, surgical management of craniofacial fibrous dysplasia remains controversial in terms of both extent and timing.[7, 8, 55–57] The ultimate major goals for surgical intervention in these patients are generally recognized as (1) preservation of key and unique functional abilities related to the craniofacial region (i.e., vision, airway patency, hearing, and the ability to chew and eat) and (2) improved cosmesis for extensive disfigurement caused by widespread involvement of the skull and face. Additional goals for less often seen conditions in the craniofacial region would include alleviation of painful symptoms related to bone overgrowth and treatment of pathologic fractures arising from the replacement of bone with fibrous tissue, resulting in loss of structural strength. The means to achieve these additional goals, however, are not as straightforward.

The timing of surgical intervention is controversial, in

large part because of the overall unpredictability of the natural course of the disease. Another consideration is whether the disease process really ever "burns out" and becomes permanently quiescent.

The dispute in recommending treatment is whether surgery should be delayed until specific key functions are imminently threatened but not yet permanently compromised or whether prophylactic surgery should be undertaken to ensure that those key functions will never be endangered. Compounding this debate are the conflicting philosophies over exactly how aggressive and extensive the surgery should be. Proponents of the aggressive approach advocate a radical resection of all diseased bone as the only way to completely eradicate the disease and prevent any possibility of recurrence or malignant degeneration. As discussed previously, craniofacial FD should be considered a unique variant of FD. Extensive and radical resection in the craniofacial region may not always be feasible and, if attempted, may cause more damage than the disease process itself. Hence, less aggressive, alternative approaches such as superficial shaving, recontouring, or curettage of the diseased bone have traditionally been advocated, reserving the radical resection of diseased bone as a last resort to salvage compromised functions.[58, 59]

The recent evolution of modern craniofacial techniques has clearly expanded the surgical options for treating patients with craniofacial FD. Improved perioperative and postoperative monitoring, greatly enhanced imaging techniques, and the multidisciplinary involvement of different surgical specialties now allow for an approach to disease in locations of the craniofacial region heretofore considered unreachable and hence untreatable. Improved three-dimensional constructs using bone grafts held in place by ever more miniaturized yet stronger fixation devices and the adaptation of microsurgical technique facilitate more extensive and complex reconstructions, as well as expand the pool of possible bone and soft tissue donor sites. Finally, advances in synthetic biomaterial technology may soon eliminate the shortage of adequate amounts of disease-free bone source as a limitation to any postablative reconstruction. Developing FD shows a predilection for specific locations within the craniofacial region. In perhaps the largest reported single institution experience with FD, 84 patients were treated at the Craniofacial Center at Chang Gung Memorial Hospital over an 18-year period, with 65% having jaw involvement.[60] In those, 80% had maxillary involvement, 15% had mandibular involvement alone, and 5% had both jaws involved simultaneously. After the maxilla, the next most commonly involved areas are the orbits and frontal bone, followed by the calvaria. FD of the craniofacial skeleton frequently crosses sutures into adjacent and contiguous bones; hence, maxillary disease often implies that there is concomitant zygoma, sphenoid, orbital, and temporal bone involvement.

In 1990, Chen and associates[55] proposed a classification scheme based on the location of the disease process and recommended what they considered was the ideal treatment plan best suited for each anatomic region (Fig. 24–6). According to this scheme, the craniomaxillofacial skeleton could be divided into four distinct zones as follows:

Zone 1, the frontal, orbital, nasal, and ethmoid bones, the zygoma, and the upper maxilla

Zone 2, the hair-bearing cranium including the parietal bone and the occipital bones

Zone 3, the central cranial base and the temporal, petrous, mastoid, and sphenoid bones

Zone 4, the teeth-bearing maxillary and mandibular alveolar bones

This scheme provides a convenient framework for a discussion of treatment at each site of the craniofacial skeleton.

Surgical Options

ZONE 1

The most critical functions within this zone involve sight and the ability to smell. How to preserve vision has long been a contentious issue in the treatment of craniofacial FD. Many authors advocate prompt prophylactic optic canal decompression, based solely on CT or magnetic resonance imaging evidence of extensive disease within the sphenoid bone, as the only way to ensure that vision will not be compromised or threatened.[61–65] Others recommend a more conservative approach, surgically decompressing only with documented evidence of vision impairment or deterioration.[66]

The mechanism by which vision can be affected is thought to be multifactoral and caused by one of three circumstances: (1) there is such extensive sphenoid bone proliferation that eventually this growth causes encirclement and encroachment of the optic canal, leading to impingement of the optic nerve; (2) there are sudden cystic changes, secondary to hemorrhage or mucocele formation within the diseased bone, causing acute direct pressure on the globe; and (3) there is substantial bone overgrowth within the eye socket causing displacement and/or compression of the globe leading to visual changes.[65] The earliest signs of visual disturbance have been described as loss of color vision, visual field changes, an afferent pupillary defect, and, occasionally, loss of central acuity, although this may occur later in the evolution of the visual loss.[61] The final physiologic pathway leading to optic nerve damage is believed to be ischemia, with disruption of axonal blood flow from external compression. This mechanism of injury has led some to believe that the visual changes are irreversible once seen, even when the nerve is subsequently adequately decompressed. Others disagree and believe that the earliest signs and symptoms of visual compromise manifest before permanent damage has occurred and that there is a limited window of time, an opportunity to intervene, before the changes become permanent.[65]

Anecdotal reports support both theories, where, on one hand, decompression did arrest further deterioration but resulted in no improvement of vision and, in other cases, there was restoration of vision after surgical intervention. Technologic advances in monitoring equipment have now provided the clinician the ability to assess blood flow within the retinal sheath itself, through the use of color Doppler imaging. A change in vision in these patients can provide early objective evidence of a compressive cause, prompting earlier surgical intervention.[61, 67]

The method of optic nerve decompression has also evolved with improvements in craniofacial surgery tech-

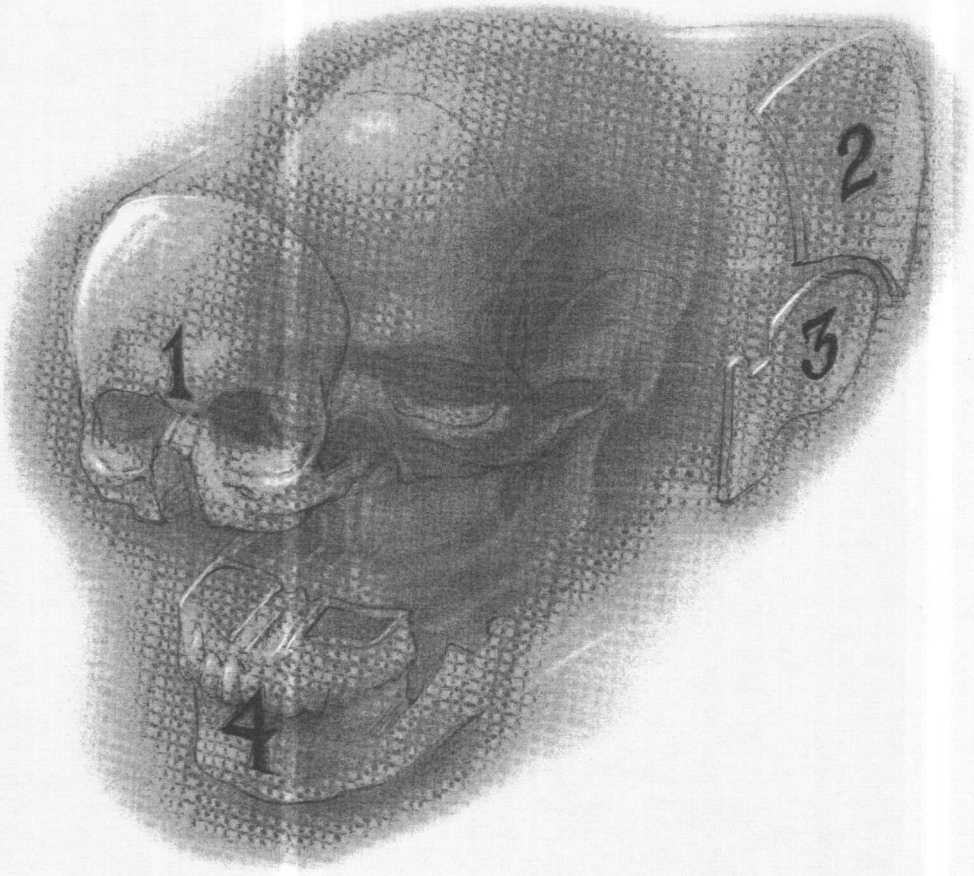

Figure 24–6. Schematic representation of the four distinct zones on the craniofacial skeleton that determine operative treatment strategy based on location of the disease.

nique. A combined intraorbital and intracranial approach is currently recommended, because the tightest portion of the canal is at the most distal end and is more easily reached from both directions. Subperiosteal frontal bone dissection extending into the orbital roof and the medial walls of the bony socket, along with dissection into the temporal hollow, facilitates a fronto-orbitotomy (Fig. 24–7). This approach through the orbital roof gives the most complete visual access to the optic canal, which is then decompressed through a combined intradural and extradural approach. The encroaching bone is carefully removed with power burrs and manual rongeurs (Fig. 24–8). Extreme caution must be undertaken with the use of power instruments during this maneuver, because the heat generated by the burrs can be easily transmitted through the adjacent bone to the neurovascular structures and can lead to a catastrophic iatrogenic blindness. It is this complication that has led many surgeons to abandon prophylactic decompression and reserve this procedure only when there is clear documentation of visual compromise. It is also with this in mind that a combined intradural and extradural approach is used at the University of Virginia. By entering the dural space and through direct visualization and protection, the optic nerve fibers can be relatively protected during the extradural decompression maneuvers.

Once the ablative surgery is completed, reconstruction is carried out using bone grafts, preferably harvested from split calvaria as free grafts or as a vascularized bone-free tissue transfer. If there has been significant orbital distortion, most often resulting in a downward vertical orbital dystopia or an outward proptosis, the globe itself must be repositioned. Bone grafts can be placed into the orbital floor and, in combination with resection of the orbital roof, can result in elevation of the globe (Fig. 24–9). Hollowing of the bony orbit can correct the proptosis as well.

Edgerton and associates advocated an alternative approach to substitute bone graft reconstruction, using the dysplastic bone itself as the source for the reconstruction.[7] They hypothesized that the bone, once osteotomized and removed, was devascularized, which prevented any further dysplastic changes or growth of the dysplastic process from occurring. The "removed, remodeled and replaced" bone had the advantage of roughly maintaining the original shape of that segment of the craniofacial skeleton, thus allowing excellent contour restoration. Other authors using this technique have noted a lack of subsequent growth in these bone segments and advise not using this technique in the growing skeleton.[68]

An approach to FD involvement of the nasoethmoidal region has been described through the use of a combined transfrontal and transfacial resection using a nasal-cheek flap to successfully relieve nasal airway obstruction. Obliterated sinuses have been hollowed out to open blocked airway passages.[69, 70]

ZONE 2

Considered not as cosmetically important as zone 1, bony contour deformities in zone 2 can be well hidden within the hair-bearing scalp, so lesions within this zone

Figure 24–7. Fronto-orbital approach to optic nerve decompression.

can be treated more conservatively. Shaving or curettage is recommended as periodically needed; and because of the limited surgery goals, extensive reconstruction afterward is rarely required. Skull defects can be covered with split calvarial bone grafts harvested from adjacent bone or covered with synthetic biomaterials that are either permanent, such as methylmethacrylate, or eventually replaced by native bone.

ZONE 3

Involvement of zone 3 is considered the most difficult or dangerous for resection of the disease. The presence of cranial nerves and large-caliber vessels and the difficulty in gaining access to this area combine to make the surgery quite problematic. FD of the temporal bone most commonly presents as progressive hearing loss, either with a conductive loss from compression of the external auditory canal or with a sensorineural loss from otic capsule encroachment or secondary cholesteatoma.[48] Other occasional presenting features of temporal bone involvement include tinnitus, trismus secondary to glenoid fossa remodeling, and facial nerve palsies. The consensus in the literature is that the hearing loss is irreversible once it occurs, but there have been anecdotal reports of hearing loss reversibility using a combination of surgical decompression and high-dose corticosteroid therapy.[71] Again, modern technical advances in cranial base surgery make lesions in this area more accessible than what was possible previously.

ZONE 4

A conservative approach has been advocated for zone 4 in the past because of the presence of the teeth. There has been a concern with extensive resection that dentures would be needed postoperatively and that these are never as functional as natural teeth. Once again, modern techniques have opened new possibilities in reconstruction that make a more aggressive approach feasible. Traditional orthognathic techniques have been applied to jaws with fibrous dysplasia, including LeFort osteotomies and sagittal split osteotomies, followed by rigid fixation using plates and screws.[58] Patients treated in this manner seem to heal without complications and have stable occlusion at long-term follow-up, good aesthetics, and no evidence of further recurrence. Adequate biocompatibility of titanium with FD in long bones has been documented, and because craniofacial bone tends to be more fibro-osseous in nature than the long bones, it is thought that this promotes the use of rigid plates and screws even more suitably.[72]

Hemimandibulectomies or subtotal mandibulectomies can be reconstructed through the use of a variety of free tissue-bone transfers; the most popular is the fibula flap or the iliac crest flap with microanastomoses to nearby facial vessels[73] (Figs. 24–10 and 24–11). After adequate healing, osseointegrated implants now substitute for dentures and allow chewing ability comparable to that of natural teeth. Again, there has been no evidence that the dysplastic process subsequently spreads into or involves the trans-

Text continued on page 380

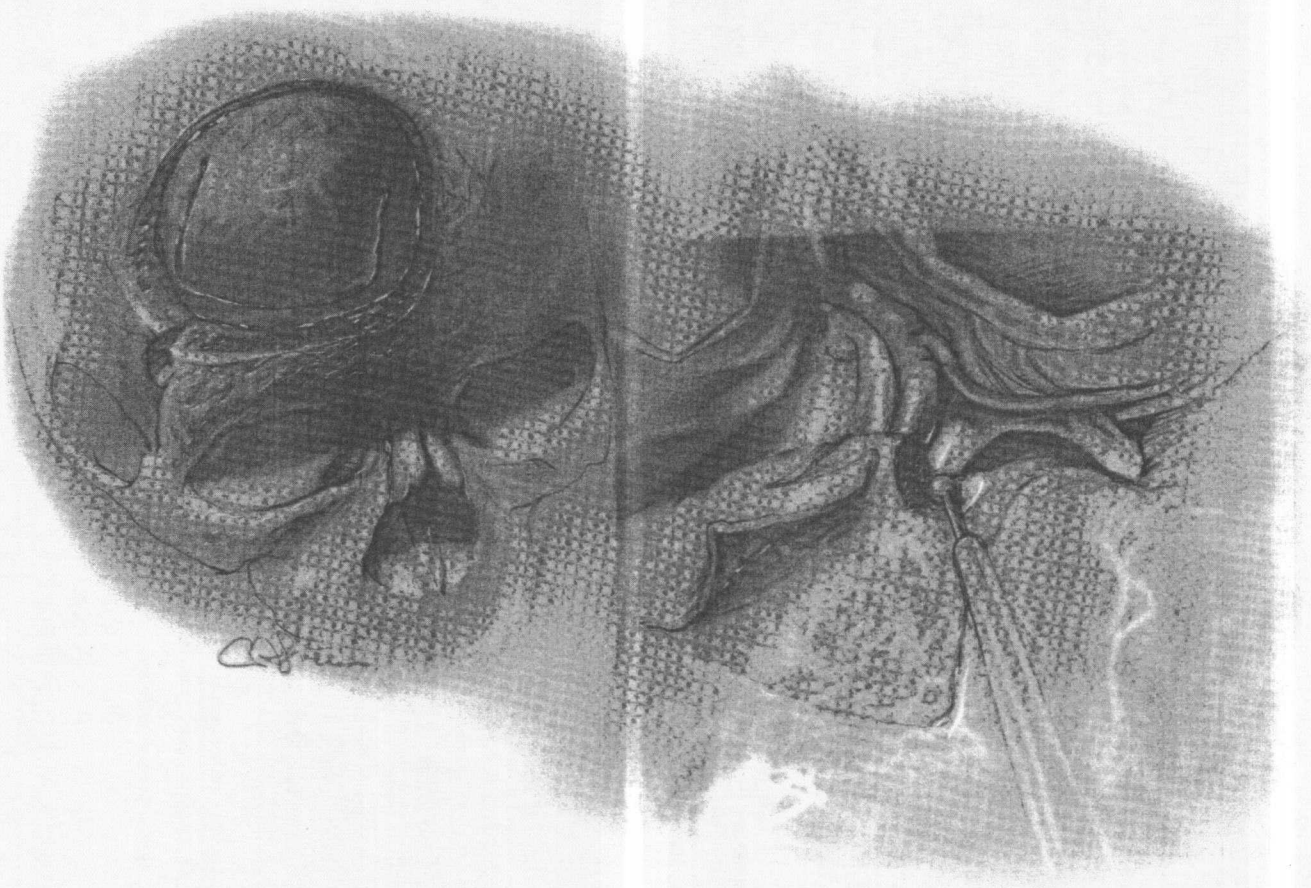

Figure 24–8. Decompression of the optic canal via an intradural approach, through careful use of power burrs and rongeurs.

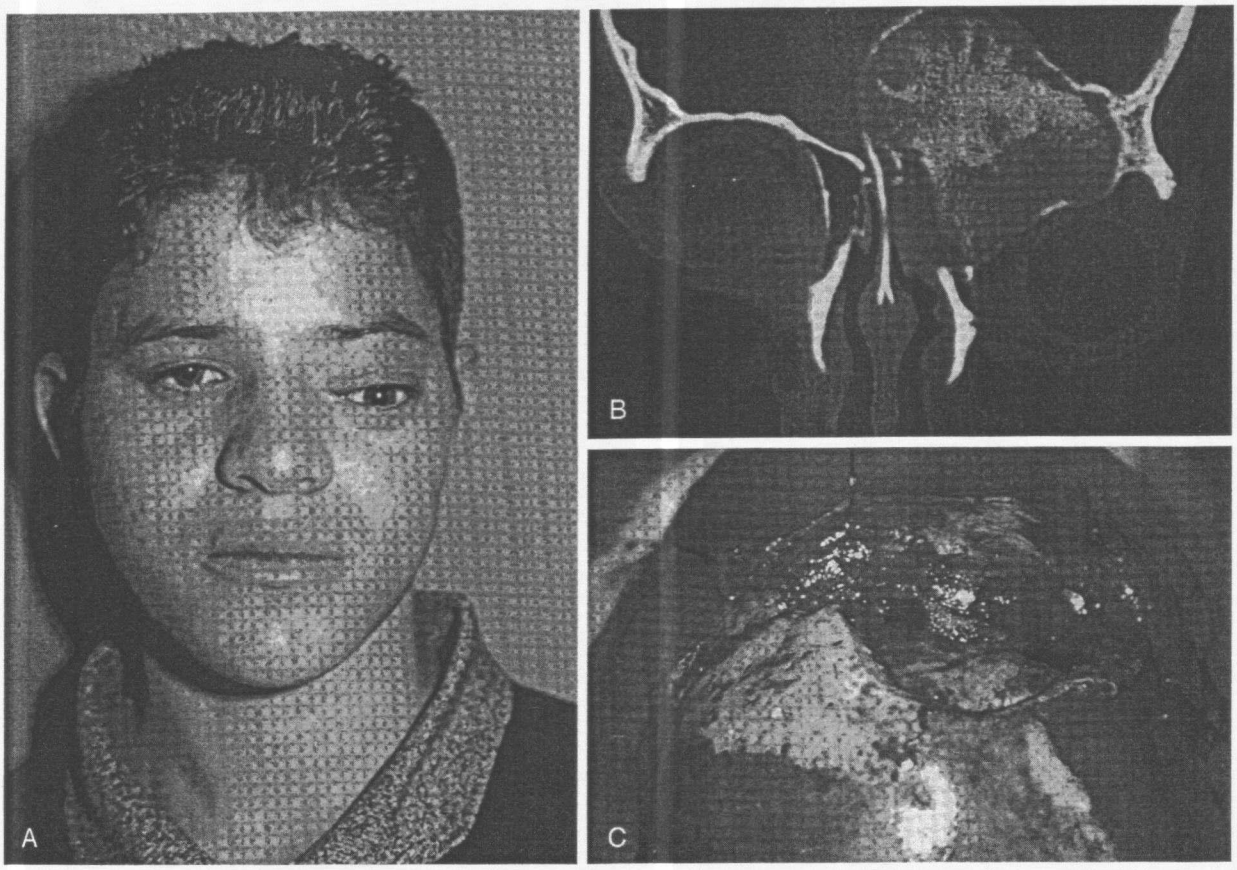

Figure 24–9. *A,* Patient with significant vertical orbital dystopia secondary to FD involvement of the orbital roof. *B,* Computed tomographic scan (coronal view) demonstrating FD of the orbital roof. *C,* Intraoperative view of frontoorbital approach.

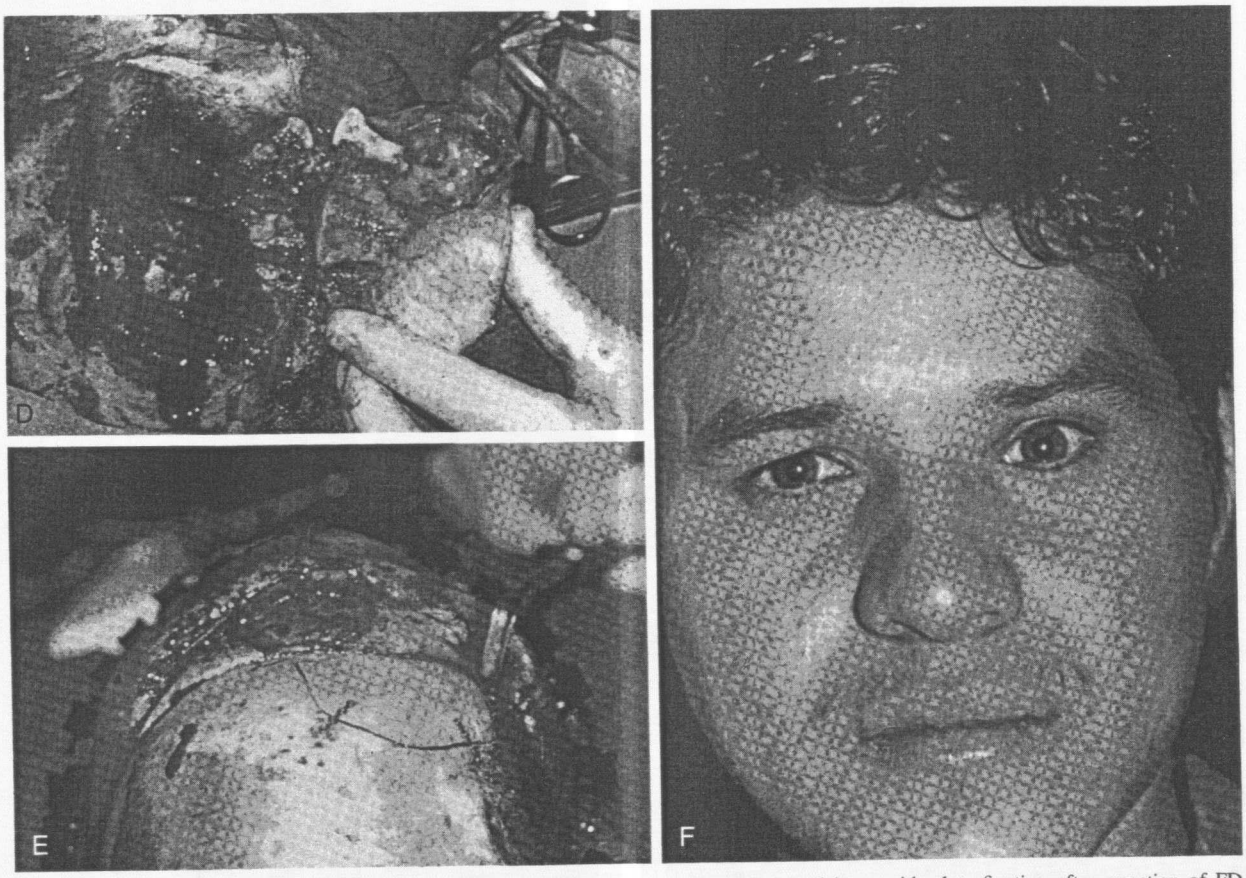

Figure 24–9 *Continued. D*, Exposed diseased bone. *E*, After orthotopic replacement of frontal bone with plate fixation after resection of FD from orbital roof. *F*, Postoperative photograph.

Figure 24–10. Schematic representation of microvascular free transfer mandible reconstruction.

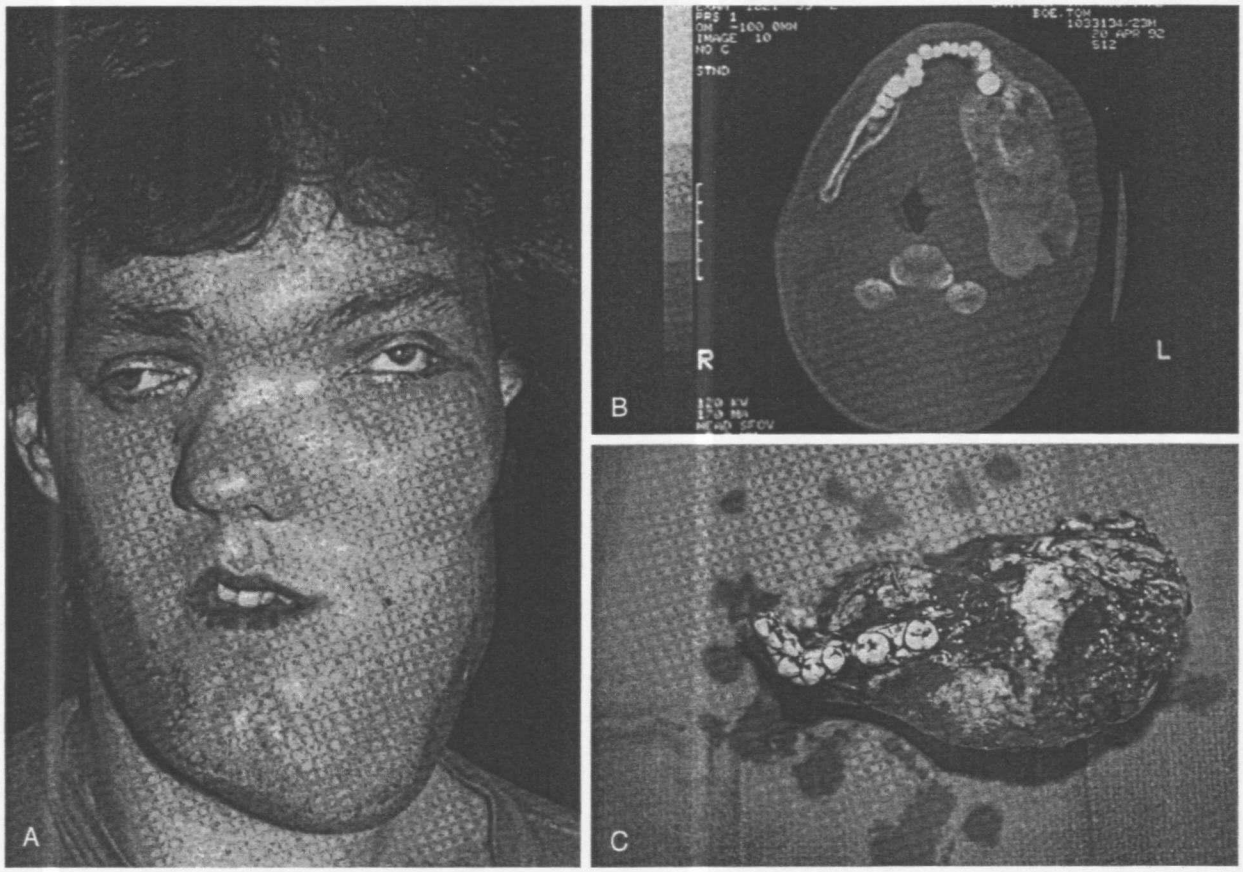

Figure 24–11. *A*, Patient with FD, involvement of the left hemimandible resulting in severe facial distortion. *B*, Computed tomographic scan of the diseased hemimandible. *C*, Exposed diseased bone via Risdon incision.

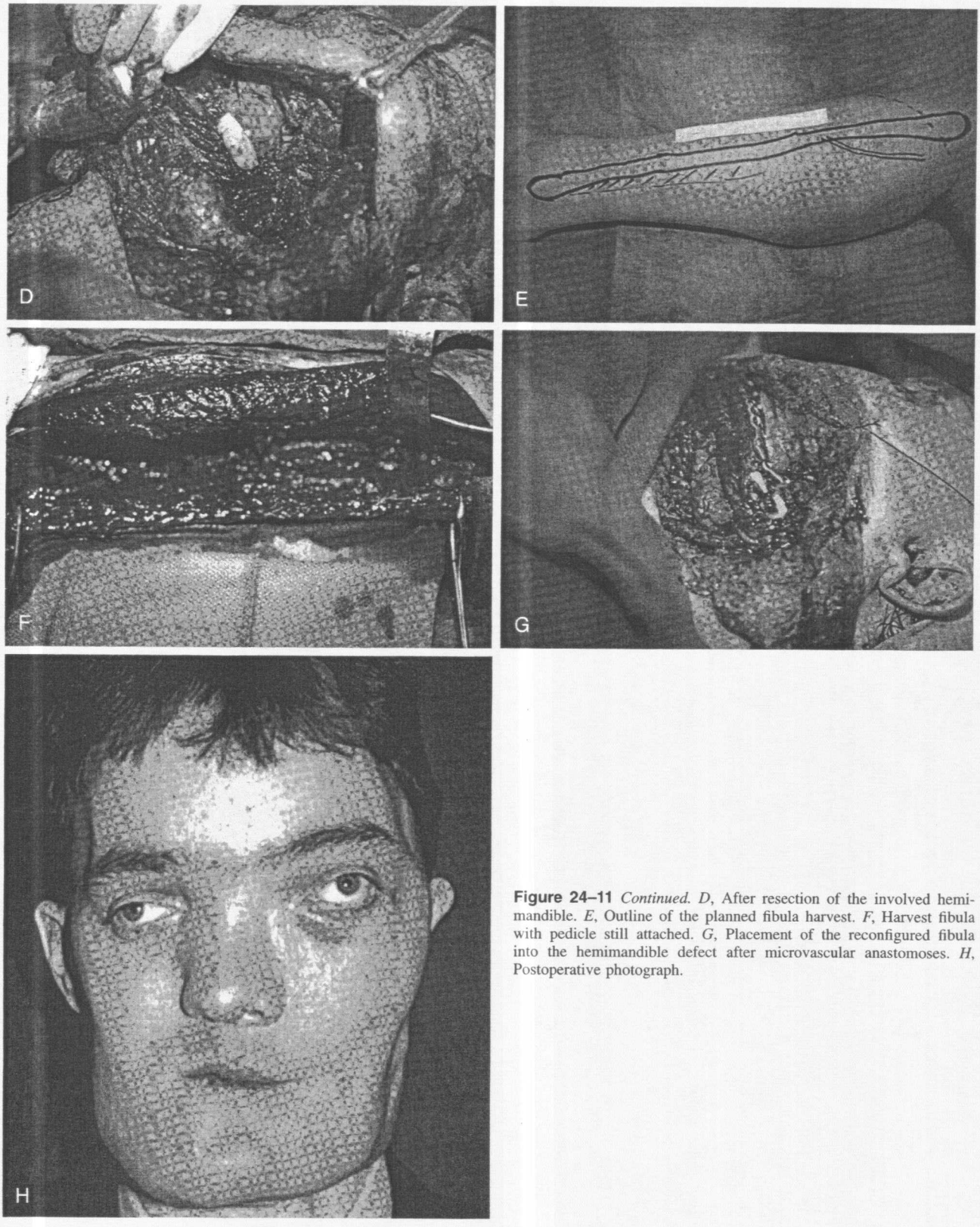

Figure 24–11 *Continued. D*, After resection of the involved hemimandible. *E*, Outline of the planned fibula harvest. *F*, Harvest fibula with pedicle still attached. *G*, Placement of the reconfigured fibula into the hemimandible defect after microvascular anastomoses. *H*, Postoperative photograph.

ferred bone flaps. Therefore, treatment recommendations in this area have evolved into wide resection of diseased bone, followed by microsurgical bone-flap mandibular reconstruction.

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